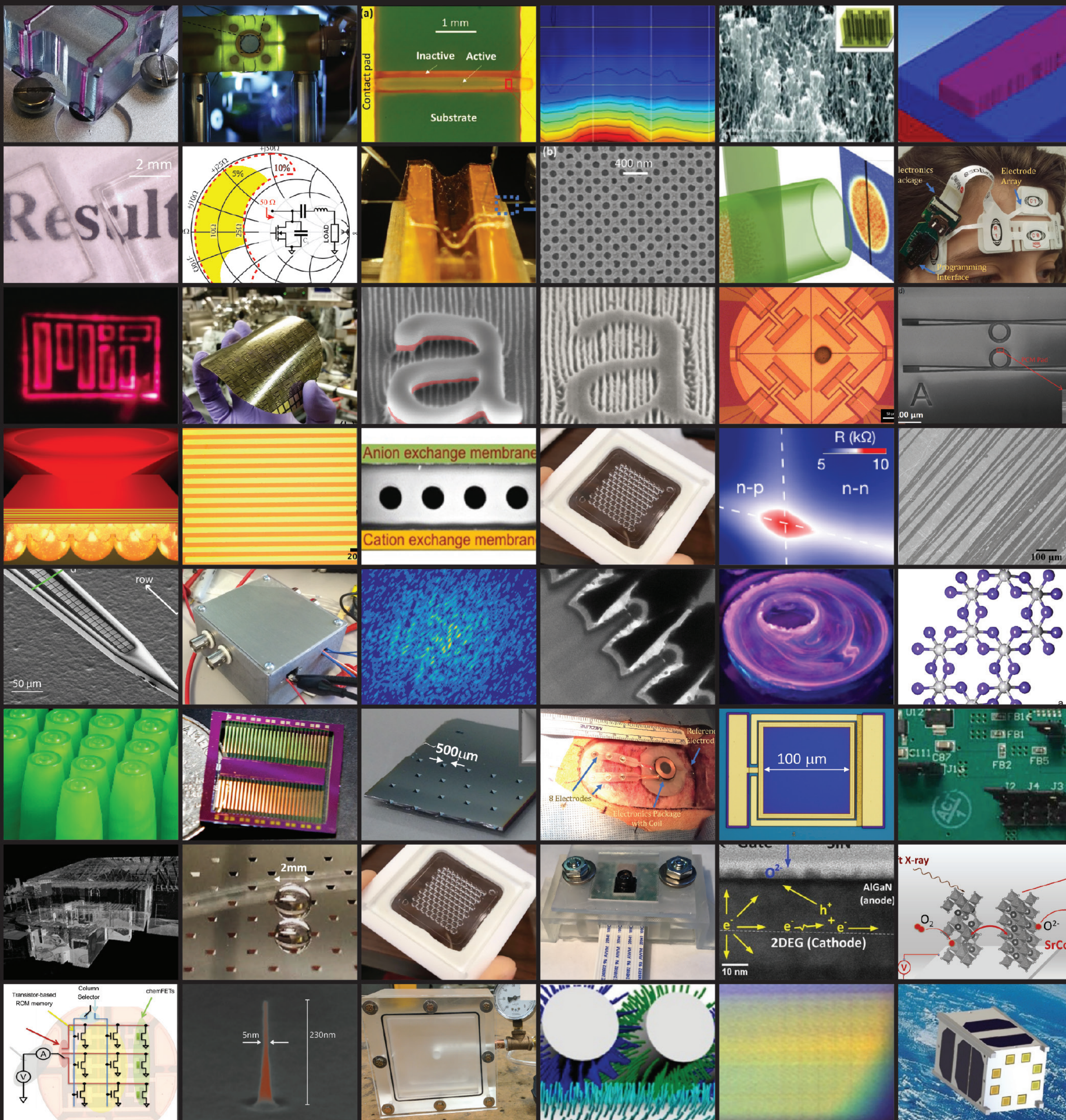


ANNUAL RESEARCH REPORT 2017

MICROSYSTEMS TECHNOLOGY LABORATORIES

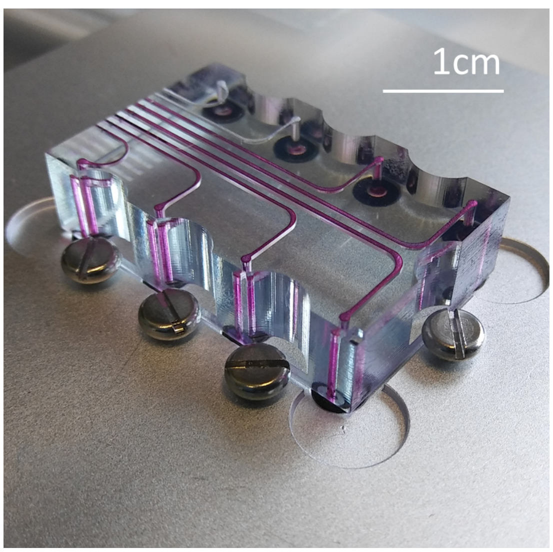
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

3-D Printed Microfluidics for Modelling Tumor Microenvironments

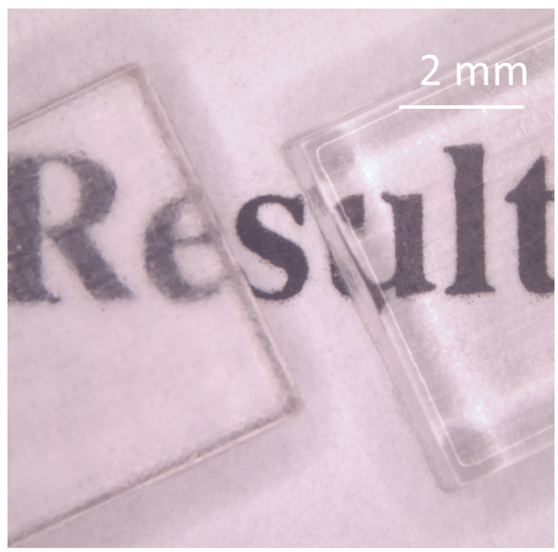
A. L. Beckwith, J. T. Borenstein, L. F. Velásquez-García
Sponsorship: The Charles Stark Draper Laboratory, Inc.

Microfluidic devices show promise as enablers of the exploration, development, and customization of medical treatments beyond traditional capabilities while saving time and cost. However, one of the principal barriers to broad application of microfluidic technologies in healthcare is related to the inherent challenges in device fabrication. Soft lithography approaches are generally restricted to planar, simple geometries and a few material options and are prone to large device-to-device dimensional variation. Current manufacturing methods for complex microfluidic devices, e.g., multi-substrate bonded micromachining, are technically challenging, time-intensive, and constrained by existing microfabrication capabilities that affect the fabrication yield. 3-D printing has the potential to significantly reduce the cost and time to manufacture microfluidics while maintaining a required level of device functionality. Additionally, 3-D printing enables rapid iteration of device designs and construction of complex microchannel features that may otherwise be difficult, impractical, or unfeasible to attain.

In this project, we are developing a Tumor Analysis Platform (TAP) that mimics interactions between tumors and the immune system in the human body, providing a microenvironment for testing the effectiveness of drugs. This microfluidic system is capable of testing treatments on tumors directly from the patient in a laboratory model to determine which therapies most effectively kill that patient's cancer. We are investigating digital light projection/stereolithography (DLP/SLA) to fabricate complex monolithic microfluidic devices that are transparent, non-cytotoxic, compatible with commonly used sterilization procedures, and, in general, suitable for biological applications. Current research has focused on exploring the biocompatibility, optical properties, minimum feature size resolution, and manufacturing repeatability of different printable materials (Figures 1 and 2). Future work will focus on implementing and characterizing different TAP designs.



▲ Figure 1: SLA 3-D printed channels with rectangular cross-sections. Channel widths as small as 275 μm were successfully printed and filled with red dye.



▲ Figure 2: Chip of 3-D printed material evidencing high transparency to visible light.

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- D. Olvera-Trejo and L. F. Velásquez-García, "Additively Manufactured MEMS Multiplexed Coaxial Electrospray Sources for High-Throughput, Uniform Generation of Core-Shell Microparticles," *Lab Chip*, vol. 16, no. 21, 4121-4132, 2016.
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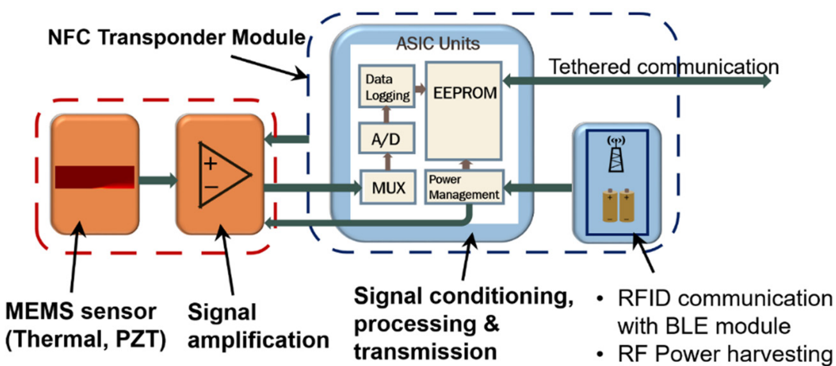
Thin-Film Transistors for Implantable Medical Devices

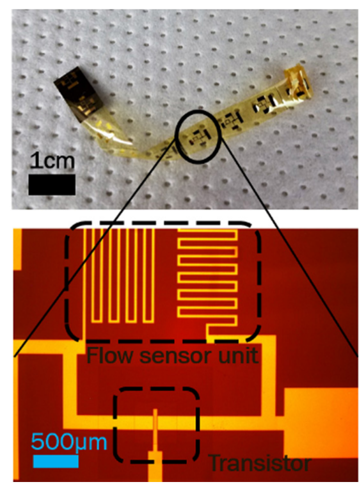
Y. Hosseini, L. F. Velásquez-García, D. S. Boning
Sponsorship: TruSpine

Miniaturization and implantation of medical devices with the ability to monitor vital body parameters can enable new opportunities for medical procedures. The implantable medical devices market is estimated to grow at 5.5% compound annual growth rate (CAGR) to reach a $55B size market by 2025. In this regard, flexible hybrid electronic systems have gained attention during the last several years for deployment on various platforms such as smart lenses, cardiac implants, and brain implants, as well as in wireless modules for communication systems integrated with these implants.

In this project, we are exploring the integration of various microsystems such as sensors, thin-film transistors (TFTs), silicon microelectronics, and radio frequency identification (RFID) modules on flexible platforms (Figure 1). The goal of this project is to fabricate the essential components of these systems in a single process to reduce the integration complexity for implementing different technologies. Our initial work has focused towards integration of TFT electronics and thermal sensors on a polyimide substrate for flow sensing applications. The TFT is fabricated as a back-gate transistor, with aluminum oxide as gate insulator and indium-gallium-zinc-oxide (IGZO) as n-type channel. The thermal flow sensor consists of a combination of a heater and a resistance temperature detector (RTD) system. The thermal flow sensor consists of Au electrodes and is the extension of one of the transistor metal layers (Figure 2). This metal layer can be further extended to serve as a signal path, bonding pad, and RFID coil. Current work focuses on characterizing, optimizing, and addressing the reliability issues related to the operation of these TFTs for signal conditioning for sensing applications.



▲ Figure 1: The design outlook for integrated microsystems for sensing applications for implantable medical devices.



▲ Figure 2: TFTs on a flexible platform with inset image showing the integrated thermal flow sensor connection to the electronic system.

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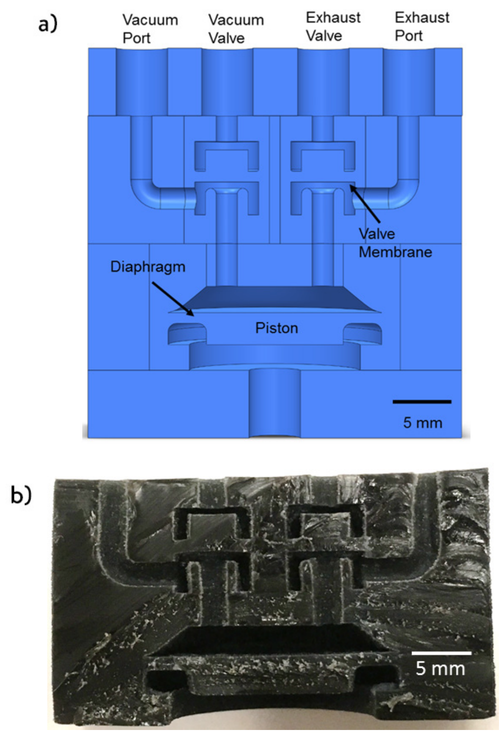
Additively Manufactured Miniature Diaphragm Vacuum Pumps

A. P. Taylor, L. F. Velásquez-García
Sponsorship: Edwards Vacuum

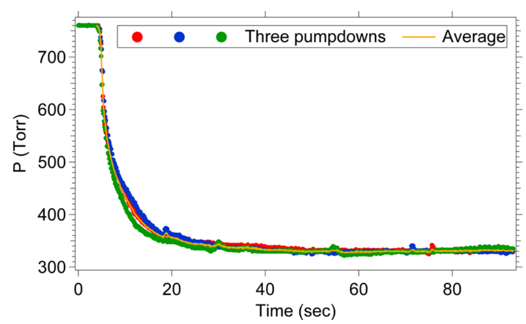
Miniaturized pumps supply fluids at precise flow rates and pressure levels in a wide variety of microfluidic systems. In particular, microfabricated positive displacement pumps that exploit gas compressibility to create vacuum have been reported as a first pumping stage in non-zero flow, reduced-pressure miniaturized systems, such as mass spectrometers. Compared to standard microfabrication, additive manufacturing offers the advantages of rapid prototyping, larger displacements for better vacuum generation and larger flow rate, freeform geometries, and a broader material selection while attaining minimum feature sizes on par with microfluidic systems (out-of-plane features in the 10-300-µm range and in-plane features in the 25-500-µm range). In addition, a number of 3-D printing techniques make possible the definition of leak-tight, closed channels or cavities, sometimes involving a second sacrificial material that is removed after printing.

Using polyjet 3-D printing technology with 42-µm XY pixelation and 25-µm layer height, a single-stage vacuum pump design with active valves and a total pumping volume of 1 cm^3 with 5% dead volume was implemented (Figure 1a). Devices were printed in the acrylate based, UV curable photopolymer TangoBlack Plus® (Shore 27A) in one piece (Figure 1b) or in two halves for ease in removing the sacrificial material. The pumps were pneumatically actuated and consistently pumped down a 1 cm^3 volume from atmosphere to 330 Torr in under 50 seconds operating at 3.27 Hz (Figure 2); from the data, the effective flow rate of the device is estimated at 8.7 cm^3/min.

The compression chamber diaphragms exhibited lifetimes approaching 20,000 cycles, while the valves' membranes have not leaked after >1-million cycles. Current work focuses on increasing the diaphragm lifetime, reducing the ultimate pressure, and improving the mass flow rate vs. pressure pump characteristics.



▲ Figure 1: (a) Design of the miniature diaphragm pump, and (b) image of a pump printed in one piece.



▲ Figure 2: Vacuum port pressure vs. time for several pump downs and average pump down characteristic, 3.27 Hz actuation.

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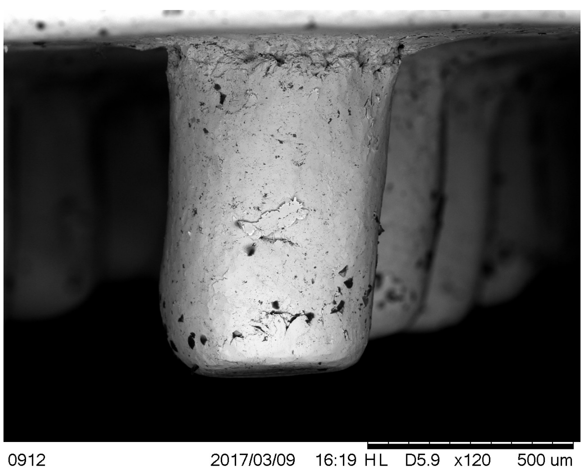
Evaluation of Lost-Wax Micromolding for Additive Manufacturing of Miniaturized Metallic Vacuum Components

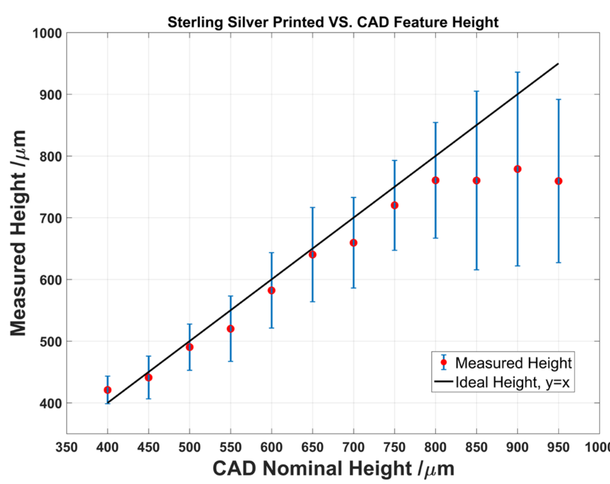
Z. Sun, L. F. Velásquez-García
Sponsorship: MIT, Skoltech Program

In contrast to traditional subtractive methods, additive manufacturing (AM) is a process of joining materials layer by layer to generate solid structures from computer-aided design (CAD) data. Benefits of AM include the reduction of the raw materials required to make the part, fast manufacturing speed, versatility, and adaptability. Furthermore, AM has the potential to enable novel designs that could not be fabricated with conventional machining practices and to enhance the capability of true 3-D micromanufacturing. Standard 3-D printing of metallic parts is done via selective laser sintering, where a coherent photon beam is used to create a solid from the melting of metal powders. However, the printed structures are coarse and porous with profusely outgassing surfaces and have electrical conductivity and mechanical strength less than those of the bulk material. Therefore, there is a need for better AM technologies to fabricate vacuum-compatible miniaturized metallic structures.

In this project, we are exploring lost-wax micromolding as an alternative AM technology for metal parts. Wax masters printed via stereolithography were duplicated in sterling silver by encasing the master in a ceramic mold, removing the wax by melting it, and filling-in with metal the cavities left within the mold after wax removal; finally, the parts are extracted from the mold and polished. An array of pillars (Figure 1) with diameter varying from 350 µm to 500 µm and height from 400 µm to 950 µm was created to characterize feature size repeatability (Figure 2). We found close agreement between the intended and cast heights for cylinders 400 µm to 750 µm tall; however for taller cylinders, the measured values are smaller than expected, and the standard deviation is also larger. This might be related to the way high aspect-ratio pillars with a small diameter solidify during casting. Further work will focus on completing the exploration of this technology to print solid, pore-free metal parts including characterization of physical properties such as roughness, thermal diffusivity, and vacuum outgassing.



▲ Figure 1: Scanning electron microscope (SEM) image of the side view of one pillar in the sterling silver resolution matrix.



▲ Figure 2: Measured lost-wax cast height vs. CAD file height in the sterling silver resolution matrix.

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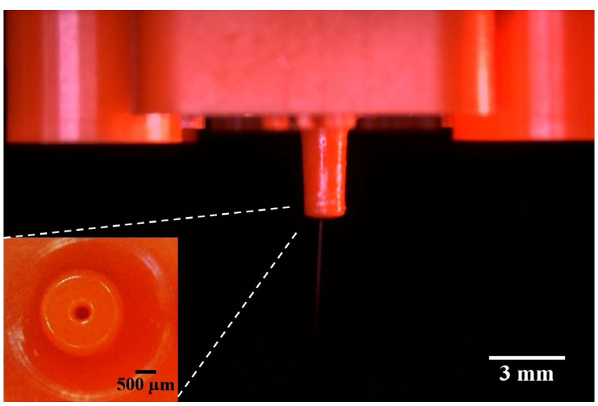
3-D Printed Multiplexed Electrospinning Sources for Large Production of Nanofibers

E. García-López, D. Olvera-Trejo, L. F. Velásquez-García
Sponsorship: MIT-Tecnológico de Monterrey Nanotechnology Program

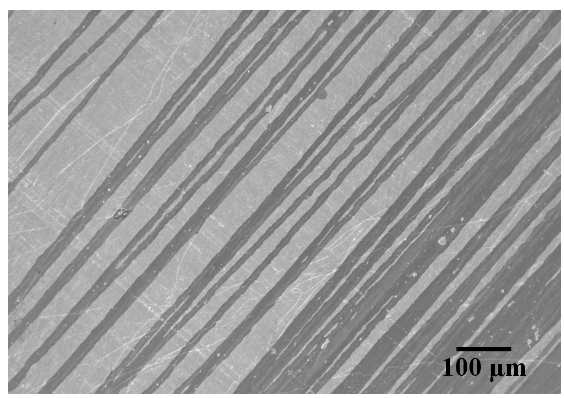
Electrospinning is a versatile process that creates ultrathin nanofibers via electro-hydrodynamical jetting. Electrospun nanofibers are used in a wide variety of biomedical (i.e., tissue healing/scaffolding, drug delivery), energy (i.e., electrodes, solar cells), and microsystem applications (i.e., sensors, batteries). Even though electrospinning is the only technique capable of generating nanofibers of arbitrarily length using a wide variety of feedstock, the throughput of an electrospinning emitter is very low, making difficult the use of these fibers in commercial products. Multiplexing the emitters, i.e., implementing arrays of emitters that work in parallel, is an attractive approach to increase the throughput of electrospinning sources without sacrificing the quality of the fibers generated. Microfabricated multiplexed electrospinning sources that achieve uniform operation at low voltage and large emitter density have been reported. However, these devices do not really solve the problem well as they are made with standard microfabrication, which is expensive and time-consuming.

In this project, we are exploring stereolithography (SLA) to create disposable electrospinning sources capable of high-throughput generation of fibers. In SLA, UV light is focused on a photopolymer while 3-D layers are created through crosslinking, making it possible to print complex three-dimensional structures. The SLA process has several advantages over competing approaches such as a higher resolution, higher quality surface, higher customization, and the creation of watertight imprints.

Devices with emitters with 300-µm internal diameter have been created (Figure 1). Measured per-emitter vs. flow rate characteristics using a PEO solution demonstrates that the arrays operate uniformly. Current research focuses on maximizing the throughput of the sources by emitter multiplexing, exploring approaches for charging up the emitted jets to produce thinner fibers, and in collecting and characterizing aligned PEO nanofibers using a drum as a collector system for tissue engineering applications (Figure 2).



▲ Figure 1: 3-D printed device with one emitter producing PEO nanofibers.



▲ Figure 2: Aligned PEO nanofibers collected using a rotating drum collector.

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Atmospheric Microplasma-Based 3-D Printing of Metallic Microstructures

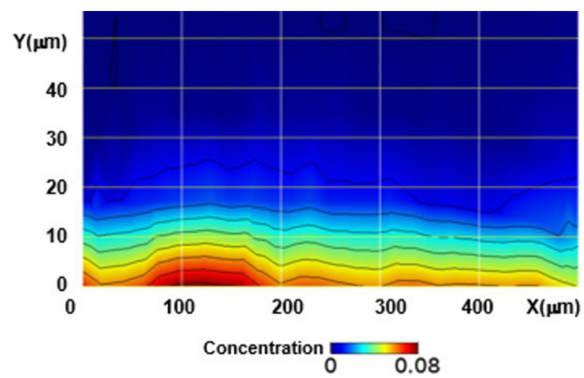
Y. Kornbluth, R. Mathews, L. Parameswaran, L. M. Racz, L. F. Velásquez-García
Sponsorship: MIT Lincoln Laboratory

State-of-the-art additive manufacturing techniques for metallic microstructures cannot yet deliver the feature resolution, electrical conductivity, and material choice flexibility needed for high-performance micro-circuits. Further, many current and proposed additive manufacturing approaches for fine-geometry metal features require high-temperature post-processing and restrict the substrate material. We aim to develop a microplasma-based sputtering system able to direct write a wide range of materials onto any substrate. We have modeled, designed, and constructed a first-generation system that sputters gold onto a substrate. By manipulating the metal at the atomic level, we retain the resistivity of bulk metal, and by sputtering the metal, we eliminate the need for post-processing or lithographic patterning.

We use a microplasma to sputter metal at atmospheric pressure, obviating the need for a vacuum. Our microplasma generator uses electrostatic fields to focus the imprints. With a suitable electrode arrangement, we can shape electrostatic fields that will guide the ionized fraction of the working gas towards a localized spot on the substrate. The directed ions will collide with other gas atoms and, crucially, with sputtered metal atoms from the sputtering target. The net force due to these collisions will indirectly guide the metal atoms towards the desired part of the substrate. This indirect electrostatic focusing not only mitigates the inherent spread of the sputtered material caused by collisions at atmospheric pressure, but also enables feature definition. In the absence of collisions, the printed line will be wider than the sacrificial cathode. By focusing the sputtered material, we achieve imprints significantly narrower than the cathode. This precludes the need to machine sacrificial electrodes as small as our desired printed lines.

Our microplasma head has a central target wire acting as the cathode, surrounded by four electrodes (Figure 1), two biased at a positive voltage (relative to the grounded target) to form the plasma, and the other two biased at a negative voltage to focus the plasma. By both pulling and pushing the plasma, COMSOL simulations predict imprints orders of magnitude narrower than the cross section of the target wire (Figure 2).

▲ Figure 1: A picture of two electrode assemblies. The target wire is installed at the center of the structure. The resulting plasma sputters metal atoms from the target, which then are carried towards the substrate by the gas flow and the electrostatic drag.



▲ Figure 2: COMSOL simulation results showing a top-down view of the distribution of sputtered material on the substrate. Only one quarter of the substrate is shown because the simulation is symmetric on the two in-plane axes. For an optimized set of parameters, simulations predict that a 15-μm-wide (full width half maximum) gold line is printed on the substrate.

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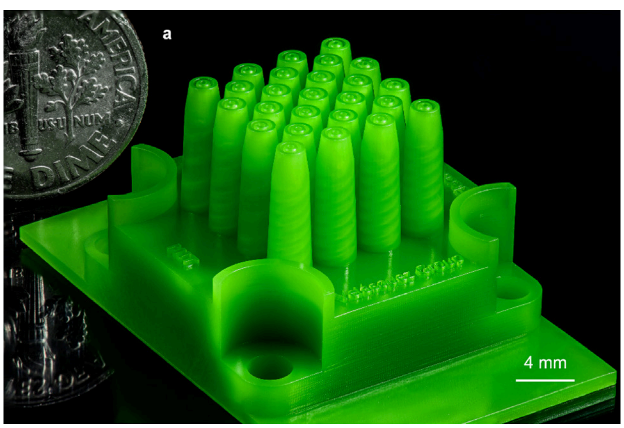
MEMS Electrohydrodynamic High-Throughput Core-Shell Droplet Sources

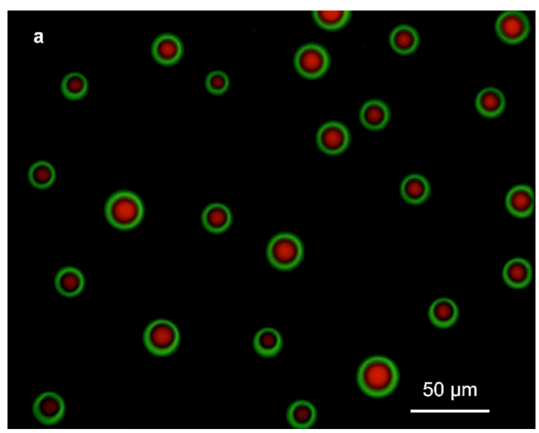
D. Olvera-Trejo, L. F. Velásquez-García
Sponsorship: MIT-Tecnológico de Monterrey Nanotechnology Program

Coaxial electrospraying is a microencapsulation technology based on electrohydrodynamic jetting of two immiscible liquids that allows precise control with low size variation of the geometry of the core-shell particles it generates. Coaxial electrospraying is a very promising microencapsulation technique because (i) it is easy to implement, (ii) it can operate at room temperature and at atmospheric pressure, (iii) it does not require a series of steps in the encapsulation process, (iv) it can generate compound droplets with narrow size distribution, and (v) it can be used to encapsulate a great variety of materials of interest to biomedical and engineering applications. State-of-the-art coaxial electrospray sources have very low throughput because they have only one emitter. Consequently, coaxial electrosprayed compound particles are compatible with only high-end applications and research.

An approach to increasing the throughput of a coaxial electrospray source without affecting the size variation of the emitted compound microparticles is to implement arrays of coaxial emitters that operate in parallel. However, no miniaturized coaxial array sources have been reported, probably due to the inherent three-dimensionality of the emitter geometry and the hydraulic network required for uniform array operation, which is at odds with the planar nature of traditional microfabrication. In this project, we demonstrated the first MEMS multiplexed coaxial electrospray sources in the literature. Miniaturized core-shell particle generators with up to 25 coaxial electrospray emitters (25 emitters·cm^{-2}) were fabricated via digital light projection/stereolithography (DLP/SLA, Figure 1), which is an additive manufacturing process based on photopolymerization of a resin that can create complex microfluidics. The characterization of emitter arrays with the same emitter structure but different array size demonstrates uniform array operation. The core/shell particles produced by these additively manufactured sources are very uniform (Figure 2); the size distribution of these compound microparticles can be modulated by controlling the flow rates fed to the emitters.



▲ Figure 1: DLP/SLA 3-D printed monolithic array of coaxial electrospinning emitters.



▲ Figure 2: Core-shell microdroplets generated by massively multiplexed MEMS coaxial electrospray sources. The feedstock was colored with fluorescent dyes to help visualize the structure of the droplets.

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Luis Fernando Velásquez-García

Principal Research Scientist
Microsystems Technology Laboratories

Micro- and nano-enabled multiplexed scaled-down systems for space, energy, healthcare, manufacturing, and analytical applications. Additively manufactured micro and nanosystems. Carbon nanotubes; electrospray, electrospinning, field emission, field ionization, plasmas, X-rays; vacuum pumps, electrical and chemical nanosatellite propulsion, plasma sensors, portable mass spectrometry, 3-D MEMS packaging, x-ray sources, tactile displays and sensors.

Rm. 39-415b | 617-253-0730 | lfvelasq @ mit . edu

POSTDOCTORAL ASSOCIATES

Anirban Basu, MTL
Erika García Lopez, MTL
Daniel Olvera Trejo, MTL
Ran Wang, MTL

GRADUATE STUDENTS

Ashley L. Beckwith, MechE
Yosef S. Kornbluth, MechE
Zhumei Sun, MechE

VISITORS

Frank Boehm, Critical Flow Technologies
Anthony Taylor, Edwards Vacuum

SUPPORT STAFF

Valerie DiNardo, Administrative Assistant

SELECTED PUBLICATIONS

A. P. Taylor and L. F. Velásquez-García, "3-D Printed Miniaturized Diaphragm Vacuum Pump," *Technical Digest 30th IEEE Conference on Micro Electro Mechanical Systems (MEMS 2017)*, Las Vegas, NV, 1292-1295, Jan. 22 - 26, 2017.

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